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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/706,567	11/12/2003	James L. Sackrison	DIA1001US	6918

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EXAMINER	
VENCI, DAVID J	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 06/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/706,567	SACKRISON ET AL.	
	Examiner	Art Unit	
	David J. Venci	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *April 1, 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9 and 11-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 11-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *04/01/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RD

DETAILED ACTION

Examiner acknowledges Applicants' reply filed April 1, 2005, which amended claims 1 and 13, and cancelled claims 10 and 15-19. Currently, claims 1-9 and 11-14 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, the step of "contacting the sample with an antibody" is indefinite because it is not clear whether/how said antibody functions in the overall method, or whether said antibody is specific for 25-hydroxy-vitamin D or vitamin D binding protein. In step c), the recitation of "an antibody" is indefinite because it is not clear whether "an antibody" corresponds to "an antibody" recited in step b).

Claim Rejections - 35 USC § 103

Claims 1-9 and 11-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Armbruster et al. (US 6,787,660) in view of Romelli et al. (US 5,382,530).

Armbruster et al. describe a method for assaying 25-hydroxy-vitamin D (see Title) in a sample of blood or blood components (see col. 6, lines 38-42) comprising the steps of: contacting the sample with an

antibody (see Fig. 7 and col. 9, lines 7-15), and determining the concentration of 25-hydroxy-vitamin D in the sample, wherein the vitamin D binding proteins are not removed from the sample before contacting the sample with an antibody (see Fig. 7 and col. 9, lines 7-15).

Armbruster et al. do not teach the step of lowering the pH of the sample to 5.5 or less to dissociate 25-hydroxy-vitamin D from vitamin D binding proteins.

However, Romelli et al. teach the step of varying the pH of a sample (see col. 7, lines 35-39) as a means for dissociating vitamins (see col. 4, line 4) from their respective binding proteins.

Therefore, it would have been obvious for a person of ordinary skill in the art at the time of invention to use the method for assaying 25-hydroxy-vitamin D, as taught by Armbruster et al., with the step of lowering the pH of the sample, as taught by Romelli et al., because Romelli et al. teach that varying pH causes ligands, including vitamins, to dissociate from their respective binding proteins, which allows these previously-bound ligands to be present during all measurement stages, which consequently results in higher assay sensitivity (see col. 4, lines 38-39) and simplification of operating procedures as compared to the prior art extractions (see col. 4, lines 56-58).

With respect to claims 2-7, it would have been obvious to a person of ordinary skill in the art to lower the pH of the blood sample to pH 5.5 or less in order to cause dissociation of 25-hydroxyvitamin D from vitamin D binding protein, since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. See *In re Aller,* 105 USPQ 233 (CCPA 1955).

With respect to claims 8-9, Romelli et al. teach the use of citrate buffers to lower the pH of a sample (see Table VI).

With respect to claim 10, Armbruster et al. teach a method for assaying 25-hydroxy-vitamin D wherein the concentration is determined by immunoassay (see Fig. 7).

With respect to claim 11, Armbruster et al. teach a method for assaying 25-hydroxy-vitamin D wherein the sample is serum or plasma (see col. 6, lines 38-42).

With respect to claim 12, the step of varying the pH of a sample as a means for dissociating vitamins from their respective binding proteins, as taught by Romelli et al., necessarily does not form a precipitate, and would be so recognized by persons of ordinary skill in the art.

With respect to claim 13, Armbruster et al. teach a method for assaying 25-hydroxy-vitamin D wherein a vitamin D tracer is used (see Abstract).

Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Armbruster et al. (US 6,787,660) in view of Romelli et al. (US 5,382,530) as applied to claims 1 and 13, and further in view of Schroeder et al., 57 METHODS ENZYMOL. 424 (1978).

Armbruster et al. and Romelli et al. teach a method for assaying 25-hydroxy-vitamin D as substantially described supra. Armbruster et al. and Romelli et al. do not teach the use of an ABEI tracer.

However, Schroeder et al. teach the use of ABEI (see p. 433) as a useful label in competitive assays (see p. 424).

Therefore, it would have been obvious for a person of ordinary skill in the art at the time of invention to include in the method for assaying 25-hydroxy-vitamin D of Armbruster et al. and Romelli et al., the ABEI

label, as taught by Schroeder et al., because Schroeder et al. teach that aminophthalhydrazides, including ABEI, are non-radioactive and consequently more convenient to handle and can be detected with high sensitivity compared to alternative labels (see p. 424).

Response to Arguments

In prior Office Action, claim 1 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite for the recitation of "wherein the vitamin D binding proteins are not removed from the sample." Applicants have amended claim 1 to add language reciting that said vitamin D binding proteins are not removed from the sample "before contacting the sample with an antibody." Applicants' amendment is sufficient to overcome this rejection. Accordingly, this rejection is withdrawn.

In prior Office Action, claims 1-13 were rejected under 35 U.S.C. 103(a) as being unpatentable over Armbruster et al. (US 6,787,660) in view of Romelli et al. (US 5,382,530). Applicants argue that there is no motivation to combine the teachings of Armbruster et al. with Romelli et al. to arrive at Applicants' invention (see Applicants' Remarks, p. 6, lines 11-14, "there is no suggestion in Armbruster or Romelli to combine these references to arrive at a competitive protein binding test for vitamin D in which the pH of the sample is lowered"). Applicants' argument has been carefully considered but is not persuasive for the following reasons:

Applicants' invention, as claimed, does not appear to recite a "competitive protein binding test for vitamin D" as suggested in Applicants' Remarks, and it is not readily apparent from the plain language of Applicants' claimed invention whether/how a competitive protein binding interaction is accomplished. Applicants' invention merely requires the steps of (a) lowering the pH of a sample, (2) contacting the sample with an antibody, and (3) determining the concentration of 25-hydroxy-vitamin D. The recited step limitations of (a) lowering the pH of a sample, (2) contacting the sample with an antibody, and (3)

determining the concentration of 25-hydroxy-vitamin D, are fully described in the combined teachings of Armbruster et al. with Romelli et al. Furthermore, Romelli et al. provide motivation to combine the teachings of Armbruster et al. with Romelli et al. to arrive at Applicants' invention by teaching that varying pH causes ligands, including vitamins, to dissociate from their respective binding proteins, which allows previously-bound ligands to be present during all measurement stages, which consequently results in higher assay sensitivity and simplification of operating procedures by not requiring multi-step extractions as taught in the prior art.

In addition, Applicants' argue that, even if the teachings of Armbruster et al. are combined with Romelli et al., the resulting method is inoperative at low pH (see Applicants' Remarks, p. 6, lines 15-18, "The competitive protein binding test... of Armbruster will not function if the pH of the sample is lowered"). This argument is not found persuasive because Applicants' specification appears to describe a similar competitive assay performed at pH 4.3 (see Specification, p. 7, "Protocol 1"). Absent objective evidence to the contrary, Examiner considers the method resulting from the combined teachings of Armbruster et al. with Romelli et al. as operative inasmuch as Applicants' claimed invention is operative.

Conclusion

No claims are allowed at this time.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Venci whose telephone number is 571-272-2879. The examiner can normally be reached on 08:00 - 16:30 (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David J Venci
Examiner
Art Unit 1641

djv

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06/03/05